UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

EPA United States Environmental Protection Agency Office of Pesticide Programs

MEMORANDUM

7/19/2017

SUBJECT: Acute Toxicity Review for Arnie, EPA Reg. No.: 3573-101

FROM: Ian Blackwell, M.S., Biologist
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TO: Eric Miederhoff, PM Team 31 / Joseph Daniels
Regulatory Management Branch I
Antimicrobials Division (7510P)

Registrant: The Procter & Gamble Company		
Decision No.: 523660	Submission No.: None	E-Sub No.: None
DP No.: 440824	Action Code: A540	
MRID No(s).: None		

Formulation from label			
PC code(s)	CAS #(s)	Active Ingredient(s)	% weight
069149	7173-51-5	Didecyl dimethyl ammonium chloride	1.65
		Other Ingredients	98.35
		Total	100.00

	RECEIVED	N/A
EPA FORM 8570-35 – Data Matrix	☐	☒
Cover letter (11/16/2016)	☒	☐
Transmittal document	☐	☒
Basic CSF	☐	☒
Proposed label	☐	☒
Beansheet	☒	☐
Acute Oral Toxicity Study (OSCPP 870.1100)	☐	☒
Acute Dermal Toxicity Study (OSCPP 870.1200)	☐	☒
Acute Inhalation Toxicity Study (OSCPP 870.1300)	☐	☒
Primary Eye Irritation Study (OSCPP 870.2400)	☐	☒
Primary Skin Irritation Study (OSCPP 870.2500)	☐	☒
Dermal Sensitization Study (OSCPP 870.2600)	☐	☒

I) **BACKGROUND**: The registrant, the Procter & Gamble Company, responded to the Agency's 5/15/2017 acute toxicity review and asked for clarification of the rationale for the assignment of acute inhalation toxicity category III for their product, *Arnie*, EPA File Symbol 3573-RNR (now 3573-101). The registrant argued that the 1:5 end-use dilution of 3573-RNR is assigned Toxicity Category III for acute inhalation toxicity, while a similar product, *Vesta*, EPA Reg. No. 3573-99, was assigned toxicity category IV for acute inhalation toxicity.

The Chemistry and Toxicology Team (CTT) conducted an acute toxicology review of EPA File Symbol 3573-RNR (concentrate and 1:5 dilution) on 2/24/2017 and revised it on 5/15/2017. For the submission, the registrant asked for a waiver of the acute inhalation toxicity study. The registrant's waiver request discussed the vapor pressure of the components of 3573-RNR, its being used in a "closed-loop" delivery system (the concentrate), and being automatically diluted 5-fold (1:5 end-use dilution) "on premise by the end user" prior to be dispensed ("to a separate, empty spray bottle" for "use as a fabric refresher product"). The registrant proposed that CTT take this submission to the Chemistry and Acute Toxicology Science Advisory Council (CATSAC) for formal assessments on two separate occasions. The waiver was denied and considered a data gap in the 2/24/2017 review of 3573-RNR. In the revised 5/15/2017 review, CATSAC waived the acute inhalation toxicity study and assigned it toxicity category III.

CTT took this case to the CATSAC again for discussion on 6/15/2017. This memo provides the revised acute toxicity review for the proposed product, *Arnie*, EPA Reg. No. 3573-RNR with the incorporation of the CATSAC decisions.

II) **FINDINGS/RECOMMENDATIONS**: In their response submitted (MRID Number 50107411) for the Agency's 5/15/2017 acute toxicity review, the registrant stated "The Arnie End Use Dilution is the product that will be used by the consumer and is equivalent to Vesta (EPA Reg. No. 3573-99)." CTT reviewed the existing registered product, *Vesta* and assigned Toxicity Category III for acute inhalation toxicity based on an acute inhalation toxicity study (MRID 49081709; D413018; 11/12/2013). For the current submission of *Arnie*, *Vesta* was found to be substantially similar to the 1:5 use-dilution of *Arnie*. Therefore, the acute inhalation toxicity data supported the registration of *Vesta* can be cited for the 1:5 use-dilution of *Arnie*.

In the 11/12/13 review (D413018), CTT indicated that the acute inhalation toxicity study (MRID 49081709) was conducted on a substantially similar product to *Vesta* and resulted in a LC_{50} greater than 1.93 mg/L with 2 animals died on Day 2 (1 of each gender out of 10 animals tested). Based on the test results, a Toxicity Category III was assigned for acute inhalation for *Vesta*. The registrant didn't agree with the Agency's decision and submitted additional acute inhalation toxicity data from a second product to support their "weight-of-evidence (WOE)" argument by then.

At the CATSAC meeting on 6/15/2017, all of the available information for the cited product, *Vesta*, and the proposed product, *Arnie*, were discussed. A unanimous decision was reached by CATSAC to keep the Toxicity Category III for acute inhalation for the 1:5 use-dilution of *Arnie*, based on the following evidence.

- The acute toxicity reviews for both *Vesta* and *Arnie* indicate the Toxicity Category III for acute inhalation endpoint.
- Although the submitted acute inhalation toxicity study (MRID 49081709) was conducted on a product that was more concentrated than *Vesta*, the Agency does not have sufficient data to conclude that *Vesta* is less toxic compared to the concentrated product. Therefore, a Category III should be assigned for acute inhalation based on the test results, unless additional data is provided to support a different category.
- The LC_{50} value for the second product was just above the end point for a category III of acute inhalation toxicity. Considering that *Vesta* is twice as concentrated as the second product, the acute inhalation toxicity may step up to a Category III.

If the 1:5 use-dilution of *Arnie* is a Toxicity Category III, then the concentrate/undiluted form of *Arnie* has to be at least a similar toxicity category, if not I or II, as the toxicity and irritation property would most likely increase with higher concentrations. The CATSAC assigned Toxicity Category III as well to 3573-RNR (concentrate) for acute inhalation toxicity. This assignment of acute inhalation Toxicity Category III is consistent with the Agency's ADBAC/DDAC Batching Guidance document (Product Reregistration Batching Guidance for Quaternary Ammonium Compounds [Cases 0350 and 3003] - Acute Mammalian Toxicity Data Requirements; 2/9/2015).

The acute toxicity profile of *Arnie*, EPA Reg. No. 3573-101(undiluted/concentrate) is currently:

Study	MRID Number	Toxicity Category	Study Status
Acute Oral Toxicity	50107407	IV	Acceptable
Acute Dermal Toxicity	50107408	III	Acceptable
Acute Inhalation Toxicity	50107409	III	Waived
Primary Eye Irritation	50107406	I	Waived
Primary Skin Irritation	50107410	III	Acceptable
Dermal Sensitization	50107406	Sensitizer	Waived

The acute toxicity profile for the 1:5 use-dilution of 3573-RNR[1] is currently:

Study	MRID Number	Toxicity Category	Study Status
Acute Oral Toxicity	49081707	IV	Cited
Acute Dermal Toxicity	49081708	IV	Cited
Acute Inhalation Toxicity	49081709	III	Cited
Primary Eye Irritation	49081710	III	Cited
Primary Skin Irritation	49081711	III	Cited
Dermal Sensitization	49081712	Nonsensitizer	Cited

[1] Cited from *Vesta,* EPA Reg. No. 3573-99

III) **PRODUCT LABELING**:

1. Precautionary Labeling for Reg. No. 3573-101/*Arnie* (undiluted/concentrate)
   A. **The Signal Word: DANGER**

B. The statement, "Keep Out of Reach of Children (KORC)", is required. It should appear immediately below the front panel signal word "DANGER".

C. The Agency's Label Review Manual (https://www.epa.gov/pesticide-registration/label-review-manual) indicates the following human-hazard precautionary statements:

HAZARDS TO HUMANS AND DOMESTIC ANIMALS:

Corrosive. Causes irreversible eye damage. Harmful if inhaled or absorbed through skin. Do not get in eyes or on clothing. Avoid contact with skin. Avoid breathing spray mist. Wear protective eyewear (goggles, face shield, or safety glasses). Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using restroom or using tobacco. Remove and wash contaminated clothing before reuse. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals.

D. **FIRST AID:**

First Aid:

If in eyes:

-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

If on skin:

-Take off contaminated clothing.
-Rinse skin immediately with plenty of water for 15-20 minutes.
-Call a poison control center or doctor for treatment advice.

If inhaled:

-Move the person to fresh air.
-If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth if possible.
-Call a poison control center or doctor for further treatment advice.

NOTE TO PHYSICIAN: Probable mucosal damage may contraindicate the use of gastric lavage.

Note to PM/CRM/Registrant: The proposed label should contain a Note to Physician which addresses the category I Primary Eye Irritant toxicity. The following statements are suggested types of information that may be included, if applicable:

- technical information on symptomatology;
- use of supportive treatments to maintain life functions;
- medicine that will counteract the specific physiological effects of the pesticide;
- company telephone number to specific medical personnel who can provide specialized medical advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. For general information on product use, etc., call the National Pesticides Information Center at 1-800-858-7378. You may also contact the poison control center at 1-800-222-1222 for emergency medical treatment information.

This product meets the Agency requirements for Restricted-Use Classification based on data that place it in toxicity category I for primary eye irritation. In lieu of assigning the product Restricted-Use classification, the product manager may consider alternatives such as face shield or goggles (to mitigate the identified hazards). Restricted-Use requirements vary depending upon use sites, e.g., institutional use, residential use, etc. Please refer to the 40 CFR §152.170 for information on Restricted-Use products.
Based upon data placing it in toxicity category I for primary eye irritation, this product meets the Agency requirements for Child-Resistant Packaging (CRP). However, the Agency does not require products that are assigned Restricted-Use status to be placed in CRP in addition to Restricted-Use Classification. CRP requirements vary depending upon use sites, e.g., institutional use, residential use, etc. Please refer to the 40 CFR, §157.22 and 157.24 for CRP requirements and exemptions. Thus, CTT recommends that the Product Manager assign this product Restricted-Use classification; if not, the registrant should place this product in CRP.

2. The precautionary labeling for the 1:5 dilution of Reg. No. 3573-101/*Arnie* is:

   A. The Precautionary Statements for the 1:5 use-dilution of *Arnie* are:

"Harmful if inhaled. Causes moderate eye irritation. Avoid contact with eyes, skin or clothing. Avoid breathing spray mist. Remove and wash contaminated clothing before reuse. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco."

B. The First Aid statements for the 1:5 use-dilution of *Arnie* are:

If in eyes:
-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

If inhaled:
-Move the person to fresh air.
-If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth if possible.
-Call a poison control center or doctor for further treatment advice.

If on skin:
-Take off contaminated clothing.
-Rinse skin immediately with plenty of water for 15-20 minutes.
-Call a poison control center or doctor for treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. For general information on product use, etc., call the National Pesticides Information Center at 1-800-858-7378. You may also contact the poison control center at 1-800-222-1222 for emergency medical treatment information.